



**RICHARD P.
FEYNMAN**
CENTER FOR INNOVATION
at Los Alamos National Laboratory

Advanced Tissue-engineered Human Ectypal Networks Analyzer (ATHENA)

March 30, 2016

Request for Information

Los Alamos National Security, LLC (LANS) is the manager and operator of Los Alamos National Laboratory (Los Alamos) for the U.S. Department of Energy National Nuclear Security Administration under contract DE-AC52-06NA25396. Los Alamos is a mission-centric Federally Funded Research and Development Center focused on solving critical national security challenges through science and engineering for both government and private customers.

LANS is opening this formal Request for Information (RFI) to gauge interest in engaging as an industry partner to LANS for collaboration in advancing the bio-assessment platform described below. Please see last section for details on submitting a Letter of Interest.

Next-Gen *In Vitro* Platform for Lead Compound and Toxicity Screening

Over the past 3+ years, Los Alamos scientists have developed a milli-scale surrogate human organ bioreactor, coupled with highly sensitive analytical technologies. Dubbed the Advanced Tissue-engineered Human Ectypal Networks Analyzer (ATHENA), the platform is a human organ construct developed for screening of lead compounds, testing of medical countermeasures, and toxicity testing. This fluidic bio-assessment platform presents a potential solution to the disadvantages of current approaches; conventional cell culture techniques lack the complexity of human organs, and the current gold standard of animal testing has proven to be an inadequate substitute. This fact is recognized by regulatory agencies such as the FDA, as well as a plethora of NGOs. However, despite impressive advances in 3D culture and engineered organs, there is still no viable alternative to cell culture or animal testing.

The ultimate potential of engineered organs will be realized by more complex, powerful, and integrated systems capable of recapitulating inter- and intra-organ signaling and dynamics, all characteristics that have been designed into Los Alamos' bio-assessment platform. ATHENA's rational design as an *in vitro* predictive platform supporting multiple human organ constructs allows for the systematic, reproducible, and quantitative screening of drugs; assessment of biological challenges; and pharmacokinetic and pharmacodynamic analysis of medical countermeasures.

To date, individual organ systems have been developed (heart, lung, liver, kidney), and two organs have been interconnected. Using related technology, the ATHENA team is currently investigating toxicology and efficacy endpoints of (1) collagen production in a skin model, and (2) cell growth

in a bone model. Future plans include development of several organs, including skin, cornea, retina, gut, nasal tissues, and immune tissues for similar and larger-scale projects.

In addition, a universal serum-free media has been under development. With the advent of multi-cellular culture systems, and the advances made in tissue models and developments in human-multi-organ-on-a-chip systems, there is a realization for the need of a 'universal' or common media that can be used to sustain multiple cell types simultaneously much akin to human blood. Blood has many important functions that are imperative for maintaining homeostasis. While blood can perform all of these functions in an animal or human, whole blood unfortunately becomes rapidly toxic in cell culture. So far no media formulation can perform all of the tasks that blood can perform; Thus far in cell culture history, much of the focus has been on supplying nutrients and regulating pH, achieved by frequent media changes to remove waste. More importantly, a significant drawback is that cell culture formulations are mostly focused on optimizing nutrients for only one cell type at a time, resulting in a very specialized media that cannot be used on other cell types. Los Alamos is currently investigating a single formula that can sustain multiple organ constructs simultaneously, allowing their intercommunication. The development of such a formula enabling the maintenance of cell types from multiple lineages will be an extremely powerful and necessary tool for the realization of multiple-cell/tissue/organ toxicological and drug testing platforms.

Potential Areas for Partnership

Accurate simulation of the spatial and functional complexity of human organs; an ability to interconnect the integrated system in a facile, real-time and high-throughput manner; platform development for portability, durability and ruggedness; and data handling will be critical factors for ATHENA's continued success. LANS has identified the following as potential areas for partnership to advance the ATHENA platform:

- Clinical validation of the bio-assessment platform for use in safety and efficacy testing;
- Bioinformatics/big data approaches to characterize, explore, validate, predict effects of substances, e.g.:
 - Epidemiological modeling,
 - Personalized medicine applications,
 - Predictive medicine applications;
- Platform deployment for, e.g.:
 - Environmental monitoring,
 - Wearable medical device;
- Additional organ module R&D for integration with the ATHENA platform, e.g.:
 - Blood,
 - Cornea,
 - Gut,
 - Nasal,
 - Oral,
 - Retina,
 - Skin;
- Studies & modeling for industry (e.g. pharmaceutical, biotech, consumer products):
 - Absorption/toxicity endpoint studies (e.g. collagen secretion),
 - ADMET PK/PD studies,
 - Combinatorial effects (local/systemic) of multiple products,
 - Effects over time or with different cohorts,

- Local/systemic effects of products administered via noninvasive routes (topical, oral, enteral, etc.),
- Modeling of host-microbiome and/or immune interactions,
- Permeation, penetration, toxicity of small molecules,
- Phenotypic or target-based screening;
- Optimization of control systems for the platform, e.g.:
 - Development of integrated data acquisition systems (DAQs) for rapid data acquisition and analysis,
 - Integration with standard clinical instrumentation/assays,
 - Optimization of the modeling and simulation of platform processes,
 - Production-level coding and integration of existing software for bio-assessment platform;
- Production-level rapid prototyping of the platform, e.g.:
 - Development of high-throughput capabilities,
 - Organs-on-chips,
 - Platform improvement,
 - Sensors and actuators;
 - Basic and exploratory science applications.

Please note this list is non-exhaustive. LANS welcomes Letters of Interest from any suitable party, and is not necessarily limited to one partner per area of interest.

LANS Intellectual Property

- Bio-Assessment Device and Method of Making the Device (LANS Ref. No. S 133,109.001, PCT App. No. PCT/US2015/052039)
- Devices For Fluid Management and Methods of Making and Using the Same (LANS Ref. No. S 133,286.001; PCT App. No. PCT/US2015/052043)
- Multi-Organ Media Compositions and Methods of Their Use (LANS Ref. No. S 133,295.001; PCT App. No. PCT/US2015/052046)
- Patterned Neuromuscular Junctions and Methods of Use (LANS Ref. No. S 133,124.001; PCT App. No. PCT/US2015/062506)
- Sample Platform and Methods of Use (LANS Ref. No. S 133,261.001; U.S. Prov. Pat. App. No. 62/212,254)
- Custom perfusion control software for fluid monitoring and management of the platform

LANS also has intellectual property portfolios in the following areas, which may be leveraged for work on the ATHENA platform: additive manufacturing, advanced materials, affinity reagents, biophysics, complex systems modeling & simulation, computational multiphysics, computational & theoretical biology, cybersecurity & cryptography, deep learning, engineered membranes, fluidics, genomics, high-throughput gene cloning, instrumentation, machine learning, novel bioassay development, protein analysis, reconfigurable soft/hardware, remote sensing, sensors, soft & composite nanomaterials, sparse signal recovery, spectroscopy, and video analytics.

Please note that the U.S. Government retains a worldwide, royalty-free, non-exclusive right to practice any LANS-owned patents and/or copyrighted software. Accordingly, any entity will have open access to LANS patents and copyrights in performance of a Government contract.

Submitting a Letter of Interest

This RFI is made without prejudice to any form of collaborative arrangement, alliance, or number of entities. *Ability and willingness to ensure compliance with U.S. Export Control law is a requirement.*

Please submit a written response on how your organization envisions utilizing this technology in partnership with Los Alamos. This may include a business or product plan, a business model, information regarding your company, or any other type of relevant information. Please properly mark any information that is considered proprietary or business-sensitive. LANS will supply a Nondisclosure Agreement to any U.S. company or person requiring it. Those companies interested in pursuing this opportunity should direct a Letter of Interest, as well as any comments or questions, to athena@lanl.gov before 11:59 MST on Friday, April 29, 2016. Download this [Request for Information \(pdf\)](#).

RICHARD P. FEYNMAN CENTER FOR INNOVATION

www.lanl.gov/feynmancenter | (505) 667-9090 | feynmancenter@lanl.gov